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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/737,445	01/10/97	DUPRE	J 223/051

18M1/0625

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EXAMINER	
NOLAN, P	
ART UNIT	**PAPER NUMBER**
1816	5

DATE MAILED: 06/25/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/737,446	Dupre
Examiner	**Group Art Unit**
Patrick J. Nolan	1816

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~or thirty days, whichever is longer~~, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-14 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-14 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Part III DETAILED ACTION

1. Claims 1-14 are pending.

2. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the GLP-1 (7-37) or GLP-1(7-36)amide, does not reasonably provide enablement for an effective fragment or analog of GLP-1 (7-37) and GLP-1(7-36)amide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to use the invention commensurate in scope with these claims.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Besides the specific polypeptides disclosed in the specification, the specification fails to provide any guidance as to how to determine the active amino acid residues within the scope of the claimed invention. These claims are drawn to GLP-1 (7-37) or GLP-1(7-36)amide and effective fragment or analogs thereof. There is no predictability in the isolation of polypeptides which fulfill the requirements of the claims because it is difficult to predict the 3-D structure of the fragments or analogues and the resulting in vivo bioactivity. Further, the term "comprises" is open ended. It would open up the amino acid sequences to include other residues. The predictability of the methods for making or isolating these fragments or analogues is limited by such factors as steric hinderance and predictability of the mutagenesis method. As applicant well knows, the predictability of changes to an amino acid sequence is practically nil as far as activities are concerned. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Applicants have not taught where the critical regions for binding and eliciting an in vivo effect are in the GLP-1 peptide. Applicant's invention relies upon peptide binding to a receptor to elicit an in vivo effect, for which the GLP-1 peptide is the ligand to. Ligand-receptor interactions are highly constrained events that require high specificity and are easily altered by substitutions to the amino acid sequence of the ligand, as evidenced by Kumar et al.(U). Kumar et al., teach that a single amino acid change in a peptide affected its ability to bind its receptor (i.e. the

MHC)(Abstract, in particular). This dramatic change in peptide-receptor, interaction demonstrates that the prior art teaches that any change in peptide amino acid sequence makes such changes unpredictable.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention and this is not sanctioned by the statute. See Ex parte Forman, 230 USPQ 546 (Bd. App. 1986).

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

3. Claims 6-9 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-9 and 14 provides for the use of the GLP-1 peptide, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 6-9 and 14 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

4. Claims 1-2, 4-14 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent 5,424,286. (A) as evidenced by Gutniak et al.,(V).

The '286 teaches the use of GLP-1(7-36) amide peptide, to treat both Type I (i.e. IDDM) and Type II (i.e. NIDDM) diabetes mellitus where the rationale for using the peptide is that it decreases the need for co-administration of insulin to treat hyperglycemia and reduce the hypoglycemic effects of insulin therapy after meal related increases of blood glucose (Column 1, lines 49-68, and References Cited on front page of patent, in particular). The '286 patent refers to the Gutniak reference cited on the front page of the patent which is titled "Antidiabetogenic Effect of Glucagon-like peptide-1 (7-36) Amide in Normal Subjects and Patients with Diabetes Mellitus". The '286 patent teaches in vivo use of the GLP-1 peptide which therefore reads on a pharmaceutical composition of the peptide.

The prior art teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5. Claims 1-5 are rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Patent 5,424,286 (A), in view of Gutniak et al., (V).

The '286 patent has been discussed supra. The claimed invention differs from the prior art only by the recitation of the administration of GLP-1(7-36)amide or GLP(1-37) at a selected time prior to ingestion of a meal.

However, Gutniak et al., teach the administration of GLP-1(7-36) amide (i.e. GLIP) 30 minutes prior to the ingestion of a meal in Type I diabetics (i.e. IDDM) and Type II diabetics (i.e. NIDDM) (Figures 2 and 3 in particular).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention was made to administer the GLP-1(7-36) amide peptide prior to the ingestion of a meal as taught by Gutniak et al., for treating insulin requiring Type I and Type II diabetes as taught by the '286 patent with the expectation that for hyperglycemic therapy to be effective it should be administered prior to a meal to give the peptide time to be absorbed and have its physiological effect just prior to the absorption of glucose by the digestion of the meal.

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants cooperation is requested in correcting any errors of which applicant may become aware of in the specification.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is (703) 305-1987. The examiner can normally be reached on Monday through Friday from 8:30 am to 4:30 pm.

8. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (703) 305-

3973. The FAX number for our group, 1816, is (703) 305-7939. Any inquiry of a general nature relating to the status of this application or proceeding should be directed to the Group receptionist, whose telephone number is (703) 308-0196

Patrick Nolan, Ph.D.
June 23, 1997

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP 1800